Chapter 5

Hepatobiliary Diseases

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I. INTRODUCTION

A. General principles

1. Hepatic disease versus hepatic failure. Multisystemic diseases (e.g., endotoxemia, hypoxemia) and toxic insults often cause hepatic disease without causing hepatic failure. Affected animals generally do not exhibit clinical signs of liver dysfunction and do not require specific therapy to support the liver. Hepatic disease in these patients is recognized by abnormally high serum hepatic enzyme activities or microscopic examination of the liver.
2. Acute versus chronic disease. Distinguishing acute liver failure from chronic liver failure on the basis of clinical signs alone may be difficult. The onset of signs in patients with acute liver failure is sudden and dramatic whereas patients with chronic liver failure usually have a history of chronic weight loss and anorexia prior to developing signs of acute disease. Because signs indicating chronicity can be missed, a liver biopsy is required to differentiate between acute and chronic liver failure.
3. Hepatocellular versus cholestatic (obstructive) disease. Liver failure, accompanied by icterus, is produced by two major mechanisms: primary hepatocyte damage (hepatocellular disease) or primary cholestasis (cholestatic disease). Cholestasis may be caused by canalicular dysfunction (intrahepatic cholestasis) or blockage of the large bile ducts.

B. Diagnosis of hepatobiliary disease. Physical examination and laboratory findings in large animals with liver failure are often similar regardless of the cause of disease.

1. Clinical findings
   a. Dermatologic signs
      (1) Icterus (jaundice) results from bilirubin deposition in tissues of animals with hyperbilirubinemia. Hyperbilirubinemia in liver failure is caused by failure of uptake, conjugation, or excretion of bilirubin.
         (a) Icterus is common in horses with acute liver failure and variably present in horses with chronic liver failure. Anorexia or fasting can cause icterus in horses with normal liver function.
         (b) Biliary obstruction is the most likely cause of icterus in ruminants.
      (2) Photodermnatitis. Phylloerythrin, produced by bacterial degradation of chlorophyll, is normally excreted in the bile. In patients with cholestasis, phylloerythrin accumulates in the systemic circulation and binds to the skin, where it acts as a photodynamic agent, causing erythema and necrosis of nonpigmented skin following exposure to sunlight.
      (3) Pruritus, attributed to the accumulation of bile salts in the skin, has been reported on occasion in horses with liver failure.
   b. Neurologic signs. Hepatic encephalopathy is a clinical syndrome that occurs secondary to liver failure and is characterized by abnormal mental status.
      (1) The pathophysiology is incompletely understood, but contributing factors include hypoglycemia, hyperammonemia, a decrease in the branched chain:aromatic amino acid ratio, and increased concentrations of mercaptans, sulfur-containing amino acids, and short-chain fatty acids in the plasma.
      (2) Clinical signs are often subtle and behavioral changes may only be obvious to the owner. Overt signs may include depression, incoordination, aimless wandering, head pressing, stupor, or coma. Frequent yawning and pharyngeal or laryngeal collapse with severe inspiratory dyspnea have been reported in

TABLE 5-1. Laboratory Findings in Hepatocellular and Cholestatic Liver Disease

Parameter	**Hepatocellular** Disease	Cholestatic Disease
Total bilirubin	Increased	Increased
Direct (conjugated) bilirubin	Mild to moderate increase	Marked increase
Indirect (unconjugated) bilirubin	Moderate increase	Normal to mild increase
Urine bilirubin	Normal to mild increase	Marked increase
Urine urobilinogen	Normal to slight increase	Absent (complete bile duct obstruction)
Alkaline phosphatase (AP)	Mild increase	Marked increase
γ-Glutamyl transferase (GGT)	Mild to moderate increase	Moderate to marked increase
Aspartate aminotransferase (AST)	Mild to moderate increase	Normal to mild increase
Sorbitol dehydrogenase (SDH)	Mild to moderate increase	Normal to mild increase

horses with hepatic encephalopathy. Excessive vocalization and tenesmus may be a feature of this neurologic syndrome in cattle.

c. Gastrointestinal signs

(1) Weight loss is a common but nonspecific finding in large animals with chronic liver disease. Anorexia and failure of hepatic metabolic functions likely contribute to the weight loss.

(2) Diarrhea, a common finding in cattle with chronic liver disease, has been attributed to increased hydrostatic pressure associated with portal hypertension. Because of the low fat content of the herbivore diet, steatorrhea is an unlikely cause of diarrhea in herbivores with liver failure.

(3) **Tenesmus,** followed by rectal prolapse, is observed in some cattle with liver disease. Hepatic encephalopathy, diarrhea, and intestinal edema secondary to portal hypertension are thought to be predisposing factors.

(4) **Ascites** is a common finding in cattle with hepatic cirrhosis, but is rarely reported in horses. Portal hypertension, and possibly hypoalbuminemia, lead to ascites.

(5) Fecal color change is unlikely in mature herbivores with biliary obstruction because chlorophyll contributes to fecal color. However, in suckling herbivores, fecal color is attributed to the presence of stercobilin (a bilirubin metabolite) and biliary obstruction can result in light feces.

(6) Recurrent subacute abdominal pain has been reported in horses with liver failure, particularly those with cholelithiasis.

d. Hematologic **signs**

(1) Bleeding diathesis. Coagulopathy leading to hemorrhage (e.g., epistaxis, prolonged bleeding from venipuncture sites) may accompany severe terminal liver iailure and is caused by inadequate hepatic synthesis of clotting factors (I, II, V, VII, IX, and X). If liver disease causes decreased bile flow to the intestines, absorption of fat-soluble vitamins, including vitamin K, will be impaired. Vitamin K_1 is required by the liver for the production of factors II, VII, IX, ard X

(2) Hemolytic **crisis.** A terminal hemolytic crisis, attributed to increased red blood cell (RBC) fragility, has been reported in horses with liver failure.

2. Laboratory **tests.** Laboratory studies can help distinguish hepatocellular and cholestatic liver disease (Table 5-1).

a. Liver enzyme studies

(1) **γ-Glutamyl** transferase **(GGT)** is predominantly associated with the cell membranes of hepatocytes and biliary epithelial cells. Other sources of GGT in horses are the pancreas and the renal tubular epithelium. However, because pancreatic disease is rare in horses, and renal disease causes an increase in urine but not serum GGT activity, increased serum GGT activity can be considered fairly specific for hepatocellular and cholestatic liver disease.

(a) Hepatocyte necrosis causes an increase in GCT activity due to leakage of this enzyme from the hepatocyte; therefore, GGT activity is almost always increased in large animal patients with acute or chronic **hepatocellular** disease.

(b) Cholestasis causes the greatest increase in GGT activity; the exact mechanism of this increase is not known, but it is usually attributed to increased production.

(2) Alkaline phosphatase **(AP)** activity can be used to evaluate the status of the liver, but this enzyme is not liver-specific. In addition to the hepatobiliaty membrane, other tissues that may contribute to increased serum AP activity include bone, intestinal tissue, and placental tissue. In horses, GCT has been shown to be a better indicator than AP of hepatobiliary and cholestatic liver disease.

(a) AP activity is usually increased in horses with chronic liver failure.

(b) In the presence of cholestasis, there is increased production and release of AP, possibly mediated through the action of bile salts. Concurrent increases in AP and GGT activity are the expected finding in large animal patients with biliary **obstruction.**

(3) Dehydrogenases [e.g., **sorbitol** dehydrogenase **(SDH),** lactate dehydrogenase **(LDH),** glutamate dehydrogenase **(GDH)**] are found in hepatocytes. Activity of these enzymes is usually increased with acute hepatocellular damage, but is often normal to below-normal in patients with chronic liver failure.

b. Serum bilirubin assessment. Hyperbilirubinemia in large animals can result from hemolysis, cholestasis, or hepatocellular disease. In horses, fasting commonly causes hyperbilirubinemia.

(1) Animals with hepatocellular disease will have increases in both conjugated and unconjugated bilirubin, with unconjugated bilirubin showing the greatest Increase.

(2) In animals with significant biliary obstruction, the magnitude of increase in conjugated bilirubin is usually greater than the magnitude of increase in unconjugated bilirubin. Horses are the exception to this rule; in this species, a conjugated serum bilirubin level that is greater than or equal to 25% of the total bilirubin indicates bile duct obstruction. Bilirubinuria, in the absence of hemolysis, is also indicative of bile duct obstruction.

c. Bile acid concentration. Bile acids are synthesized in the liver from cholesterol. They are present in high concentrations in the portal circulation, are extracted by the liver with high efficiency (greater than 90%), and are transported via the biliary tree. An elevated bile acid concentration has high specificity for diagnosis of liver disease, but cannot be used to differentiate between hepatocellular and obstructive disease.

(1) Hepatocellular disease. Bile acid concentrations are increased in patients with hepatocellular disease as a result of decreased extraction from the portal circulation.

(2) Obstructive liver disease. Bile acid concentrations are increased in patients with obstructive liver disease as a result of decreased biliary excretion.

d. Dye excretion tests. Sulfobromophthalein and indocyanine dyes can be used to assess hepatobiliary transport. Because these dyes are difficult to obtain, serum bile acid measurements have replaced dye excretion tests for evaluation of liver function in large animals.

e. Miscellaneous laboratory assessments

(1) Serum prothrombin time **(PT).** The serum PT may be increased as a result of decreased synthesis of cloning factors in patients with liver failure.

(2) Plasma triglyceride concentration. The plasma triglyceride concentration may be increased in horses and cattle with hepatic lipidosis.

(3) Plasma ammonia concentration. The plasma ammonia concentration may be increased due to decreased conversion of ammonia to urea in the liver. The degree of elevation of the plasma ammonia level is poorly correlated with the severity of the hepatic encephalopathy.

(4) Glucose level. Hypoglycemia due to anorexia, decreased hepatic glycogen stores, and decreased hepatic gluconeogenesis occurs in large animals with liver failure.

(5) Plasma protein level. The liver produces most plasma proteins, including albumin and α and β globulins. Hypoalbuminemia is uncommon in patients with liver failure, but decreased α and β globulin concentrations have been reported in horses with chronic liver failure. In contrast, γ globulin concentrations are increased due to chronic antigenic stimulation.

3. Other diagnostic modalities

a. Hepatic ultrasound. Ultrasound examination of the liver is used to diagnose hepatomegaly, cholelithiasis (with or without biliary dilatation), and space-occupying lesions in the liver.

b. Percutaneous liver biopsy is used to determine the presence and cause of liver disease.

(1) Procedure. Samples may be obtained blindly or with ultrasound guidance and should be placed in formalin for histology and appropriate media for bacterial culture.

(2) **Contraindications.** The procedure is relatively safe, provided that the coagulation profile is normal. A liver biopsy should be avoided when liver abscesses are suspected.

C. Treatment of hepatobiliary disease. Supportive care is most appropriate in patients with acute hepatic failure because the liver has a tremendous regenerative capacity. Treatment of patients with chronic liver failure is generally unrewarding because regeneration is restricted by fibrosis that bridges lobules. Supportive medical therapy may entail the following measures:

1. Management of hepatic encephalopathy

a. Sedation. Restless or convulsing animals should be sedated. Xylazine (0.5–1.0 mg/kg) and diazepam (0.05–0.4 mg/kg) are effective sedatives in most patients; drug dosages may have to be adjusted because most sedatives and anticonvulsants are metabolized by the liver.

b. Minimization of the production or absorption of toxic metabolites

(1) Mineral oil is used to decrease absorption of toxic protein metabolites produced by enteric bacteria.

(2) Lactulose (0.3 ml/kg orally once every 6 hours) can be used to decrease ammonia absorption from the gut, and neomycin (10–100 mg/kg orally once every 6 hours) may be given to decrease the production of ammonia by intestinal microflora. However, these two treatments are costly and may cause diarrhea.

(3) Diet. Proper dietary management is crucial. A diet that provides 30–40 kcal/kg body weight (BW) in the form of low-protein, high-energy feeds rich in branched-chain amino acids (e.g., milo, sorghum, beet pulp) has been recommended for all horses with liver failure, but particularly those with signs of hepatic encephalopathy.

(a) A mixture of two parts beet pulp and one part cracked corn in molasses fed at 2.5 kg/100 kg BW/day is usually divided into six or more feedings.

(b) Oat or grass hay should be substituted for high-protein alfalfa or legume hay.

2. Intravenous fluid therapy. 5% Dextrose (2 ml/kg/hour) should be used for the first 24 hours in patients that are hypoglycemic or exhibiting signs of hepatoencephalopathy. If fluid therapy is to be continued for more than 24 hours, 2.5%–5% dextrose in lactated Ringer's solution should be substituted. In anorexic patients, potassium chloride can be added to fluids at a rate of 20–40 mmol/kg.

TABLE 5-2. Recommended Oral Dosages of Corticosteroids for Patients with Chronic Active Hepatitis

	Dosage
	1.5 mg/kg twice daily
	1.0 mg/kg twice daily
	1.0 mg/kg once daily
12–16	0.5 mg/kg once daily

3. Vitamin supplementation

a. Vitamin K_1 (40–50 mg/450 kg BW subcutaneously once weekly) is indicated to prevent coagulopathies.

b. Vitamin B_1 and folic acid may also be administered once weekly.

4. Antimicrobial therapy. Ideally, antimicrobial therapy should be based on culture and sensitivity results. Empiric therapy for suppurative cholangitis usually includes the administration of a β lactam and an aminoglycoside, or trimethoprim–sulfamethoxazole. Metronidazole should be added if anaerobic infection is suspected.

5. Therapy for chronic active hepatitis. A variety of diseases can cause chronic active inflammation of the liver.

a. Corticosteroids. Administration of corticosteroids may benefit patients with chronic active hepatitis. A recommended dosage schedule is given in Table 5-2.

b. Colchicine. Theoretically, colchicine will reverse hepatic fibrosis, but the efficacy of this drug in horses is not known.

II. HEPATOBILIARY DISEASES OF HORSES

A. Hepatobiliary diseases of adult horses

1. Serum hepatitis (Theiler's disease) is a complication of equine-origin biologic administration [e.g., tetanus antitoxin (TAT)].

a. Epidemiology. Sporadic cases, epidemics, and seasonal (early summer and fall) patterns have been described. Even in epidemics, the morbidity rate is low, ranging from 2%–18% for inoculated horses. The mortality rate is high, approximately 66%.

b. Patient profile and history

(1) Patient profile. Lactating mares appear to be at highest risk due to the practice of administering TAT at parturition. Foals rarely develop the disease, even when treated with the same batch of TAT used to treat the dams.

(2) History. Affected horses usually present with a history of neurologic signs 4–10 weeks after the administration of equine-origin biologics.

c. Clinical findings. Signs of acute hepatic failure (e.g., photodermatitis, hepatic encephalopathy, icterus, inappetence, pica, yawning) are commonly observed. Fever may occur in 50% of patients.

(1) Weight loss, ventral edema with jugular pulsations, and severe dyspnea were reported as atypical signs in one outbreak.

(2) Subclinical disease characterized by increases in serum enzyme activity has been documented in TAT-treated mares and foals.

d. Etiology

(1) A viral agent, similar to the hepatitis B virus that affects human beings, is the proposed but unproven cause of serum sickness. Affected horses that had not been previously inoculated usually have had contact with treated horses, suggesting contact transmission.

(2) Theiler's disease has also been attributed to a type III (immune complex–mediated) hypersensitivity reaction.

e. Diagnostic plan

(1) History and **clinical findings.** Icterus and neurologic dysfunction, coupled with a history of recent administration of TAT or another equine-origin biologic, suggests a diagnosis of serum hepatitis.

(2) Liver biopsy. Histologic examination of liver samples obtained antemortem or postmortem usually reveals moderate to severe hepatocellular degeneration throughout the lobule, with the most severe changes occurring in the centrilobular and zona intermedia regions.

f. Therapeutic plan. Supportive medical therapy is the key to treating horses with serum hepatitis, but the mortality rate is high. Recovery in treated horses may take 4–21 days. Survivors of postvaccinal epidemics have no clinical evidence of lasting hepatic disease.

g. Prevention. Vaccination of the mare with tetanus toxoid 30 days before parturition is a safer approach to tetanus prophylaxis than the routine use of TAT in recently foaled mares and foals.

2. **Pyrrolizidine** alkaloid (PA) toxicosis can occur when horses graze contaminated pastures or hay. PA-containing plants are unpalatable and will only be consumed by horses if growth is so heavy that the toxic plants cannot be separated from normal forage, or if pastures are overgrazed. The plants remain toxic in hay, including pelleted and cubed products, and silage.

a. Patient profile and history. Horses and cattle are equally susceptible to PA toxicosis, whereas sheep and goats are quite resistant. Because signs are often delayed, liver failure may not be recognized until 1 year or more after the contaminated feed source has been removed.

b. Clinical findings. Clinical signs of PA toxicosis are those described for liver failure and commonly include weight loss, icterus, and hepatic encephalopathy. Photodermatitis and diarrhea are occasionally seen.

c. Etiology and pathogenesis

(1) Etiology. Plants containing PA include Senecio, *Amsinckia, Crotalaria,* and *Heliotropium.*

(2) Pathogenesis. Following gastrointestinal absorption, the PAs are carried via the portal circulation to the liver and metabolized by hepatic **microsomal** enzymes to more toxic **pyrroles.**

(a) The pyrroles may cause cross-linking of DNA and an antimitotic effect; hepatocytes that cannot divide become **megalocytes** as cytoplasm expands without nuclear division.

(d) Pyrroles also cause centrilobular and periportal hepatocellular necrosis. Ultimately, severe hepatocellular fibrosis and biliary hyperplasia ensue.

d. Diagnostic **lan**

(1) Serum Biochemical profile. In acute cases, dehydrogenase activity is increased. CGT and AP activity is consistently increased. Increased concentrations of bile acids and direct and indirect bilirubin are also seen. Hypoalbuminemia and clotting abnormalities occur terminally.

(2) **Liver** biopsy will reveal a triad of fibrosis, bile duct proliferation, and **megalocytosis,** which is almost pathognomonic for PA toxicosis, although similar changes have been reported in cases of aflatoxicosis. Modest hepatocellular changes and bile duct hyperplasia indicate a fair prognosis; extensive fibrosis bridging portal areas implies a guarded prognosis.

e. Therapeutic plan. There is no specific treatment for PA toxicosis. Affected horses should be removed from contaminated pastures.

(1) Horses with overt clinical signs of liver failure usually die within 5–10 days.

(2) Supportive therapy is indicated for horses with mild signs and reversible liver lesions.

f. Prevention

(1) PA toxicosis is prwented by avoiding exposure of horses to contaminated hay or pasture. The growth of *Senecio* can be controlled by cultivation or herbicide spraying.

(2) Sheep, which are more resistant to poisoning, are sometimes used to graze *Senecio*-infested pastures.

3. **Cholelithiasis**

a. Patient profile and history

(1) Patient profile. The mean age of affected horses is 11 years (range, 5–23 years). No breed or sex predilection has been reported.

(2) History. Affected horses are presented with a history of repeated bouts of mild abdominal pain over periods of up to 1 year.

b. Clinical findings. Recurrent abdominal pain and fever spikes, accompanied by weight loss and icterus, are characteristic clinical signs. Signs of hepatic encephalopathy have been reported in a few affected horses.

c. Etiology. The etiology of cholelithiasis in horses is not known. Bacterial infection ascending from the duodenum to the common bile duct, leading to bile stasis, has been proposed as a cause. Salmonella has been cultured from the biliary tree of some affected horses.

d. Diagnostic plan

(1) Hematologic work-up. Hematologic findings in horses with biliary obstruction usually include leukocytosis with neutrophilia, hyperproteinemia, and hyperfibrinogenemia.

(2) Serum biochemical profile. Common serum biochemical abnormalities reported in affected horses include marked increases in serum activity of cholestatic liver enzymes (i.e., CGT, AP) and moderate increases in dehydrogenase activity. Conjugated hyperbilirubinemia and bilirubinuria are also seen.

(3) Abdominocentesis. Because recurrent colic occurs in horses with cholelithiasis, abdominocentesis is usually performed. Peritoneal fluid in affected horses may be orange-tinged, increased in volume, and have cytologic findings that suggest chronic active inflammation.

(4) Ultrasonography can assist with antemortem diagnosis of cholelithiasis. Typical findings are hepatomegaly, marked dilatation of bile ducts, and hyperechoic areas (choleliths), which cause acoustic shadowing.

(5) Liver biopsy, with samples submitted for bacteriology and culture, is a useful ancillary diagnostic test in equine patients with cholelithiasis.

(a) Although histologic findings are nonspecific, they can provide useful prognostic information; extensive periportal fibrosis, bile duct proliferation, biliary stasis, and hepatocyte necrosis usually indicate a poor prognosis.

(b) Bacterial culture and sensitivity results can be used to guide antimicrobial therapy.

e. Therapeutic plan

(1) Supportive therapy should be employed in horses with signs of liver failure.

(2) Antimicrobial therapy is indicated to treat secondary bacterial cholangitis. Because enteric bacteria are most commonly involved, penicillin and an aminoglycoside or penicillin and trimethoprim–sulfamethoxazole are indicated.

(3) Cholelith removal

(a) Cholelithotripsy and choledochotomy have been attempted, but poor surgical outcomes are common because of extensive hepatic fibrosis, multiple unremovable stones throughout the hepatobiliary tree, secondary choleperitoneum, and postoperative Salmonella-induced colitis.

(b) Bile acid therapy, used to dissolve choleliths, has not been employed in horses because dissolution of calculi takes many months and most calculi in horses are not composed of cholesterol, a requirement for the effectiveness of bile acid therapy.

f. Prevention. There are no specific recommendations for the prevention of cholelithiasis because the predisposing factors have not been identified.

4. Hyperlipidemia is a disorder of lipid metabolism.

a. Patient profile and history

(1) Patient profile. Hyperlipidemia occurs primarily in ponies and donkeys. Although the disease is uncommon in horses, it has been recognized with some irequency in miniature horses. Mares in late gestation or early lactation are

more frequently affected than stallions or geldings. Animals that are in good to obese condition seem to be predisposed to the disease.

(2) **History.** Many equids with hyperlipidemia have a history of recent stress (e.g., transportation, inclement weather, changes in diet).

b. Clinical findings

(1) Initial clinical signs include inappetence, lethargy, reluctance to move, and incoordination and weakness. Mild intermittent abdominal pain and decreased intestinal motility and fecal output are common findings. Diarrhea develops terminally. Prior to death, most affected animals exhibit neurologic signs. The interval between the first appearance of signs and death is usually less than 10 days.

(2) Other variable and nonspecific findings include pyrexia, tachypnea, icterus, congested mucous membranes, and ventral subcutaneous edema.

c. Etiology and pathogenesis

(1) **Etiology.** The theory that hyperlipidemia occurs solely as a complication of a primary disease process has recently been refuted. Concurrent disease has only been identified in one third of cases. Examples of such diseases include intestinal parasitism and other gastrointestinal disorders, hyperadrenocorticism, laminitis, and metritis.

(2) **Pathogenesis.** In hyperlipidemia, lipolysis of adipose tissue is induced by activation of **hormone-sensitive lipase** during times of negative energy balance or stress. However, the lipolysis is unregulated because of resistance of the hormone-sensitive lipase to the inhibitory action of insulin. Insulin resistance is induced by factors such as breed, obesity, pregnancy, and lactation.

(a) Unregulated lipolysis results in the release of **free fatty acids** into the circulation in amounts that overwhelm the liver's oxidative ketogenic capacities. The excess free fatty acids are esterified to **triglycerides** in the liver, which are subsequently secreted as **very low-density lipoproteins (VLDLs).** Therefore, patients with hyperlipidemia have increased plasma triglyceride and VLDL concentrations.

(b) Circulating triglycerides and VLDLs are hydrolyzed by **lipoprotein lipase,** which is located in capillary endothelium of adipose tissue, skeletal, and cardiac muscle.

(i) Free fatty acids released from the hydrolyzed triglycerides are used as an energy source in muscle or stored in adipose tissue as triglycerides.

(ii) Direct uptake of VLDLs into the peripheral tissues by cells or the reticuloendothelial system may explain the fatty infiltration of organs identified in affected equids at necropsy.

d. Diagnostic plan

(1) **Plasma triglyceride assessment.** The plasma of severely affected equids is lipemic, with a milky appearance. Plasma triglyceride concentrations commonly exceed 400 mg/dl.

(2) **Serum biochemical profile.** Other biochemical findings include hypoglycemia, metabolic acidosis, evidence of liver failure (e.g., increased serum liver enzyme activity, hyperbilirubinemia, hyperammonemia, prolongation of the PT), and azotemia. Laboratory findings should be interpreted with care because lipemia can interfere with some clinical chemistry tests.

e. Therapeutic plan

(1) **An attempt should be made to treat any underlying disease.**

(2) **The energy balance should be corrected and maintained.**

(a) **Diet.** Highly palatable feedstuffs (e.g., newly cut grass, leafy hay, rolled grains, or meals with added molasses) should be offered. Enteral feeding of slurries made from alfalfa cubes, or pelleted hay and electrolyte solutions, should be administered via nasogastric tube 4–8 times per day in anorectic patients.

(b) **Intravenous fluid therapy.** In patients with compromised gastrointestinal function, 5% dextrose should be administered as a constant intravenous infusion at a rate of 1–2 ml/kg/hour; balanced electrolytes should be added if fluid therapy is continued for more than 24 hours.

(c) **Appetite stimulants.** Anabolic steroids and vitamins may be used as appetite stimulants and to assist hepatic function. Glucocorticoids are contraindicated because they induce the activity of hormone-sensitive lipase.

(d) **Reduction of energy drain**

(i) **Abortion** is an option in pregnant mares with hyperlipidemia; however, retained fetal membranes and laminitis are likely sequelae.

(ii) **Weaning.** Foals should be weaned from lactating mares with hyperlipidemia.

(3) **Plasma lipid concentrations should be lowered.**

(a) **Exogenous insulin** (30–80 IU protamine zinc insulin administered intramuscularly twice daily) is used to inhibit the activity of hormone-sensitive lipase. Insulin should be used in conjunction with oral or intravenous glucose to promote the esterification of fatty acids in adipose tissue. However, insulin resistance may render this treatment ineffective.

(b) **Heparin** (100–200 IU intravenously twice daily) has been employed in an attempt to lower triglyceride concentrations by increasing the activity of lipoprotein lipase. However, recent research has shown that lipoprotein lipase activity is near maximum in ponies with hyperlipidemia, so heparin may act only to increase the risk of coagulopathy.

f. Prevention

(1) Attempts should be made to reduce stress and prevent obesity in susceptible animals.

(a) Exercise and controlled feed intake may improve insulin sensitivity in ponies and reduce the risk of hyperlipidemia.

(b) Feed intake of animals being transported should be closely monitored and high-quality, energy-rich concentrates should be provided during transportation.

(c) Drastic weight reduction programs for conditions such as laminitis should be avoided in at-risk equids.

(2) Due to the rapid progression of the disease, owners of at-risk animals should be advised to seek immediate veterinary attention for animals that are lethargic and anorectic.

5. Other disorders. The following disorders are uncommon causes of hepatic failure:

a. Chronic active hepatitis
b. Hepatocellular and cholangiocellular carcinomas
c. Bacterial cholangitis (caused by *Salmonella* infection)
d. Hepatic abscess
e. Parasite migration
f. Chronic hepatotoxicosis resulting from exposure to aflatoxins, kleingrass, or alsike clover
g. Overzealous steroid administration

B. Hepatobiliary diseases of foals

1. Tyzzer's disease

a. Patient profile and history

(1) **Patient profile.** Tyzzer's disease is observed in foals 7–42 days of age.

(2) **History.** Usually there is a history of sudden death. The client may describe a foal that is in shock and exhibiting neurologic signs.

b. Clinical findings. The disease has a short clinical course (hours to 2 days); sudden death without clinical signs is common. If there are clinical signs, they are nonspecific and include depression and anorexia that rapidly progress to recumbency, seizures, and coma. Foals may be hypothermic or febrile (temperatures can range from 39°C–41°C) and marked icterus develops terminally.

c. Etiology. Tyzzer's disease is caused by *Bacillus piliformis,* a gram-negative, spore-forming, motile bacillus.

d. Diagnostic plan

(1) Laboratory studies. Clinical pathologic data are nonspecific and include marked increases in liver-derived serum enzyme activity, marked hypoglycemia, and neutropenia or neutrophilia.
(2) Postmortem examination. Findings include severe icterus, generalized petechiation, and marked hepatomegaly. The cut surface of the liver usually contains multiple scattered foci of necrosis 1–2 mm in diameter. *B. piliformis* is difficult to culture. A diagnosis is usually confirmed by demonstrating long, slender bacilli in silver-stained formalin-fixed liver sections.

e. Therapeutic plan. Suspected early cases may respond to treatment, but the prognosis for recovery is generally poor. Intravenous antimicrobial therapy with penicillin and an aminoglycoside and supportive treatment for acute liver failure are recommended.
f. Prevention. There are no specific control measures for this sporadic disease. Because the dam may be the source of infection, subsequent foals should be closely monitored for signs of disease.

2. Ferrous fumarate poisoning (toxic hepatic failure). Foals that received a microorganism inoculum containing ferrous fumarate before nursing developed liver failure at 2–5 days of age. Hepatic encephalopathy, marked hyperbilirubinemia, hyperammonemia, and prolongation of the PT were consistent findings in affected foals. Postmortem examination of affected foals revealed small, reddish-brown livers with evidence of massive hepatocellular necrosis. The nutritive supplement containing this iron preparation is no longer available.

3. Other disorders. The following disorders are occasionally associated with hepatic failure in foals:
a. Congenital equine herpesvirus 1 infection
b. Septicemia *(Actinobacillus equuli)* infection
c. Endotoxemia
d. Perinatal asphyxia
e. Portocaval shunts
f. Biliary atresia
g. Administration of parenteral nutrition (associated with cholestasis and hepatic disease)
h. Gastric ulcers and duodenitis in older foals (associated with duodenal strictures leading to bile stasis and secondary cholangitis)
i. Hepatic abscesses (possibly as a sequela of septic omphalophlebitis)

III. HEPATOBILIARY DISEASES OF RUMINANTS

A. Hepatobiliary diseases of adult ruminants

1. Hepatic abscesses
a. Patient profile and history
(1) Patient profile. Ruminants of all ages, breeds, and sexes may be affected. Liver abscesses are common in dairy and beef cattle fed diets high in carbohydrates and low in roughage. Approximately 40% of feedlot cattle may have liver abscesses; feedlot cattle 6–24 months of age are affected most often.
(2) History. A history of rumenitis or reticuloperitonitis is common.
b. Clinical findings
(1) Subclinical disease. Most liver abscesses are incidental findings at postmortem. The only clinical sign may be the fact that the rate of gain is usually reduced by more than 3.5% in animals with subclinical disease.
(2) Clinical disease is characterized by weight loss, anorexia, depression, and decreased milk production. Intermittent fever spikes can occur. Some cattle may be reluctant to move or lie down and experience pain when pressure is applied behind the right posterior rib cage.
(3) Clinical findings related to sequelae

(a) Caudal vena cava thrombosis can occur following erosion of the caudal vena cava by a liver abscess, resulting in one of three clinical syndromes
(i) Sudden death (due to septic shock following rupture of the abscess)
(ii) Epistaxis, hemoptysis, and anemia caused by widespread pulmonary thromboembolism and rupture of an aneurism
(iii) Severe dyspnea and diffusely abnormal lung sounds following nonfatal rupture of a pulmonary abscess
(b) Bile duct occlusion. Large abscesses may occlude the bile duct, leading to icterus and photodermatitis.
(c) Diffuse peritonitis following rupture of the abscess into the abdominal cavity

c. Etiology and pathogenesis
(1) Etiology. The primary etiologic agent of hepatic abscesses in cattle is *Fusobacterium* necrophorum. Other bacterial etiologic agents include Actinomyces *pyogenes*, Streptococcus, Staphylococcus, and Bactemides.
(2) Pathogenesis. In cattle, erosion of the ruminal epithelium secondary to grain overload is thought to be the most common mechanism for F. *necrophorum* colonization of the liver.

d. Diagnostic plan
(1) Laboratory studies. Findings supporting a diagnosis of liver abscess in cattle include neutrophilia, hyperfibrinogenemia, hyperproteinemia, and hyperglobulinemia. Anemia [evidenced by a decreased packed cell volume (PCV), RBC count, and decreased hemoglobin] may result from blood loss secondary to hemoptysis or from chronic inflammation. Serum liver enzyme activities are usually normal because abscesses are focal and encapsulated.
(2) Liver biopsy is of little use for diagnosis because focal lesions are easily missed. Biopsies may cause rupture of an abscess and septic peritonitis.
(3) Ultrasound examination can confirm the presence of hepatic abscesses.

e. Therapeutic plan. Long-term penicillin or tetracycline therapy is indicated for treatment of affected animals; however, affected cattle, particularly those with caudal vena cava thrombosis, have a very poor prognosis and are usually not treated.
f. Prevention
(1) Gradually introducing concentrate feeding over a 3- to 4-week period and providing adequate amounts of coarse hay (1 kg/head/day), will reduce the incidence of hepatic abscesses in feedlot cattle.
(2) Feeding a total mixed ration and long-stemmed hay (2.3 kg/head/day) with rumen buffers (e.g., sodium bicarbonate, magnesium oxide) may reduce incidence of liver abscesses in dairy cattle.
(3) Antimicrobials can be added to beef cattle rations to decrease the incidence of liver abscesses (e.g., chlortetracycline at 70 mg/kg/head/day or oxytetracycline at 75 mg/kg/head/day).

2. Fascioliasis (liver fluke infestation)
a. Patient profile. Liver flukes cause disease in cattle, sheep, and goats.
b. Etiology and pathogenesis
(1) Etiology. Fascioliasis in domestic ruminants is caused by the trematodes ***Fasciola hepatica, Fasciola gigantica,*** and ***Fascioloides magna.***
(a) *F.* hepatica occurs primarily in the Gulf Coast and western states.
(b) F. gigantica is found in Hawaii.
(c) F. *magna* occurs in the Gulf Coast states, Great Lakes region, and northwestern states where grazing domestic ruminants share pastures with deer, elk, and moose (natural hosts of the parasite).
(2) Pathogenesis. All have an aquatic snail (limnaeid snails) as an intermediate host. The life cycle of F. hepatica and F. gigantica are similar; F. magna completes the full life cycle only in its natural hosts (deer, elk, moose).
(a) Fluke eggs hatch in the water to miracidia, which develop through sporocyst, redia, and cercaria stages after the miracidia penetrate the snail intermediate host. Cercariae later emerge from snails, encyst as metacercariae on herbage, and are eaten by the final host.

(i) *F.* hepatica infestation occurs in livestock grazing low-lying swampy pastures, flood irrigation areas, and pastures adjacent to slowly moving streams. These habitats favor the propagation of the snails that act as the intermediate hosts for liver flukes. In the Gulf Coast states, warm, wet winters and springs favor massive proliferation of snails. hatching of fluke eggs, and development of cercariae. Most fluke transmission occurs between February and July; transmission ceases when summer heat and drought results in the death of snails and metacercariae. Mature egg-laying flukes, susceptible to flukicides, are present in the fall.

(ii) In the Pacific Northwest, fluke transmission may be delayed because freezing weather causes death of metacercariae and snails.

(b) Metacercariae encyst in the small intestine. Young flukes migrate through the gut wall and peritoneal cavity and reach the liver in 4–6 days. They migrate in the liver for 4–6 weeks, enter the bile ducts, and mature to egg-laying adults 10–12 weeks postinfection. F. hepatica can survive for many years in sheep and shed thousands of eggs per day; cattle develop resistance and usually eliminate flukes within 1 year.

(i) Acute F. hepatica disease is caused by invasion of the liver by massive numbers of immature flukes. Severe hepatic parenchymal damage and massive hemorrhage into the peritoneal cavity cause liver failure and severe blood loss anemia.

(ii) Chronic F. hepatica disease is attributed to activity of adult flukes in the bile ducts. Cholangitis, biliary obstruction, and biliary fibrosis are responsible for weight loss and icterus. Anemia and hypoproteinemia result from blood-sucking adult flukes.

(iii) F. *gigantica*-induced disease. The pathogenesis is similar to that of disease caused by F. hepatica.

(c) Anaerobic necrotic tracts produced by migrating liver flukes may trigger proliferation of latent Clostridium novyi or Clostridium hemolyticurn spores. Exotoxins produced by these bacteria are responsible for black disease in sheep (see III A 3) and bacillary hemoglobinuria in cattle (see III A 4).

c. Clinical findings

(1) F. *hepatica.* Disease caused by F. hepatica infestation can be acute or chronic.

(a) Acute disease due to F. hepatica is common in sheep and goats, but rare in cattle due to natural and acquired immunity. Outbreaks last 2–3 weeks and signs include anorexia, depression, weakness, pale mucous membranes, dyspnea, ascites, abdominal pain, and dry feces. Acute fascioliasis causes high mortality in sheep.

(b) Chronic disease, Chronic fluke infestation causes significant production losses in cattle and sheep.

(i) Clinical manifestations in sheep include progressive weight loss, pale mucous membranes, intermandibular edema, ascites, and, occasionally, icterus.

(ii) Chronic disease is the only manifestation of fascioliasis in cattle. Reported signs include poor body condition, decreased milk yield, and anemia.

(2) *F. gigantica* infestation causes signs similar to those of F. hepatica infection.

(3) *F. magna* infestation causes acute, rapidly fatal disease in sheep and goats, and chronic disease in cattle as a result of unrestricted fluke migration. *F. magna* infestation is subclinical in cattle because flukes are rapidly encapsulated by fibrous tissue.

d. **Diagnostic plan**

(1) Serum biochemistry and hematology. Serum biochemical and hematologic findings include severe anemia, hypoalbuminemia, eosinophilia, and increased serum liver enzyme activity in acute disease. Chronic disease is characterized by anemia, hypergammaglobulinemia, and conjugated hyperbilirubinemia.

(2) Fecal sedimentation is the standard method for diagnosing F. hepatica infection in cattle. The technique is time-consuming and infections may be missed because low egg counts are common and immature flukes do not produce eggs. A new fecal test (Flukefinder®), based on the use of two sieves, is simple to perform in the field and reduces sample processing time.

(3) Enzyme-linked immunosorbent assay (ELISA) tests for serologic diagnosis of liver fluke infestation are being developed. These tests are limited by their low sensitivity and specificity and the difficulty of using these tests to differentiate between current infection and prior exposure.

(4) Postmortem examination

(a) Findings in acute cases include an enlarged hemorrhagic liver covered by fibrin strands, a large volume of serosanguinous peritoneal fluid, and excessive numbers of immature flukes (more than 1000) in the liver parenchyma.

(b) In chronic cases, the liver is small and fibrotic with more than 200 adult flukes in the bile ducts.

e. Therapeutic plan. Two drugs are available for treatment of fascioliasis in North America, and two experimental drugs (triclabendazole and netobimin) are being developed.

(1) **Clorsulon** (7 mg/kg orally) is a narrow-spectrum flukicide with no activity against gastrointestinal nematodes. Clorsulon is more than 99% effective against adults and 96% effective against late immature flukes.

(2) Albendazole (10 mg/kg orally) is a broad-spectrum flukicide, effective against both liver flukes and gastrointestinal nematodes. Albendazole is 75%–90% effective against adults and 33% effective against late-stage immature flukes.

f. Prevention

(1) Livestock should not be grazed in high-risk areas during periods of peak transmission. Snail habitats should be fenced or drained if possible.

(2) Molluscicides (e.g., copper sulfate) may be of value when applied to small snail habitats, but toxic effects on nontarget species is a problem.

(3) Flukicides should be used strategically.

(a) A summer treatment in the Gulf Coast states with a broad-spectrum flukicide (or a narrow-spectrum flukicide combined with an anthelmintic) will remove a high proportion of drug-susceptible mature and late-stage immature flukes and peak numbers of hypobiotic nematode larvae.

(b) Annual fall treatments are sufficient in the Pacific northwest because they will remove adult fluke burdens before the winter nutritional stress period.

3. Black disease (infectious necrotic hepatitis) occurs worldwide in areas where liver flukes are endemic and sheep are raised.

a Patient profile and history

(1) Patient profile. Black disease affects sheep and, to a lesser degree, cattle.

(2) History. The chief complaint is of sudden deaths in the herd or flock.

b. Clinical findings. The usual clinical manifestation is sudden death. Affected animals show signs for only a few hours; the sudden onset of a fever (40°C–41°C) that rapidly progresses to hypothermia, signs of toxemia, and respiratory distress may be observed.

c. Etiology and pathogenesis

(1) Etiology. Black disease is usually caused by the interaction of Clostridium novyi type B bacteria and immature F. hepatica liver flukes.

(2) Pathogenesis. Spores of *C.* novyi present in normal liver may germinate when hepatic tissue is damaged by migrating immature liver flukes. (Other forms of liver damage, including biopsy, can also trigger the condition.) Sporulating bacteria produce potent necrotizing α and β toxins that damage the liver parenchyma, causing toxemia and death.

d. Diagnostic plan. Diagnosis is usually made at postmortem. There is evidence of recent liver fluke migration and toxemia (i.e., the presence of serosanguinous fluid in the thoracic cavity and pericardial sac and subendocardial and

subepicardial hemorrhages). Bacilli can be observed in necrotic tracts in the liver on histologic examination.

e. Therapeutic plan. Therapy is not usually feasible, but affected animals can be treated with intravenous fluids and massive doses of sodium penicillin (44,000 U/kg intravenously every 6 hours). Specific antisera are not commercially available.

f. Prevention. Control of fluke infection through pasture management and treatment of individual animals should be instituted together with vaccination against C. novyi type B. Vaccinations should be given in the late spring and early summer preceding the seasonal occurrence of black disease. In endemic fluke areas, cattle are vaccinated every 6 months.

4. Bacillary hemoglobinuria is an acute, highly fatal, toxemic infectious disease affecting cattle and, occasionally, sheep. It is caused by Clostridium hemolyticum (*Clostridium novyi* type D), a soil-borne anaerobe that, under hypoxic conditions, multiplies in hepatic tissue and produces a potent necrotizing and hemolytic exotoxin. Clinical signs include fever, hemoglobinuria, rapid death, and a large anemic infarct in the liver.

5. Hepatic lipidosis is associated with fat cow syndrome of dairy cattle (see Chapter 9 I G), pregnancy toxemia (protein energy malnutrition) of beef cattle (see Chapter 9 I H), and pregnancy toxemia in ewes and does (see Chapter 9 I F).

6. Hepatotoxicosis

a. Aflatoxicosis

(1) Patient profile. Aflatoxicosis affects cattle and small ruminants, although these animals are less susceptible than monogastric animals and poultry. Young animals are more susceptible than adults to the toxic effects of aflatoxins. Aflatoxicosis occurs in areas with high rainfall, humidity, and temperatures.

(2) Clinical findings

(a) Acute aflatoxicosis causes signs of liver failure resulting from hepatic necrosis.

(b) Chronic aflatoxicosis is associated with reduced weight gain, poor feed conversion, and decreased milk production (as a result of aflatoxin's adverse effect on the rumen microflora). Affected animals also have an increased susceptibility to infection.

(3) Etiology and pathogenesis. Aflatoxins are produced primarily by *Aspergillus* species in stored grains; these fungi can occasionally invade cereal crops prior to harvest if climactic conditions favor growth.

(a) *Aspergillus flavus* is the primary producer of four major **aflatoxins (B_1, B_2, G_1, and G_2)** and several related compounds. Aflatoxin B_1 is the most abundant aflatoxin and is converted in lactating animals to aflatoxins M_1 and M_2, which are concentrated and secreted in milk. Aflatoxin M_1 is as toxic and carcinogenic as aflatoxin B_1, thereby posing a hazard to humans consuming contaminated milk.

(b) Acute, massive exposure to aflatoxin causes hepatocellular necrosis through a direct toxic effect.

(4) Diagnostic plan

(a) Acute **aflatoxicosis**

(i) Histopathologic evaluation of a liver biopsy sample or liver tissue obtained postmortem will reveal hepatocellular necrosis, hemorrhage, vacuolation, fatty infiltration, and megalocytosis.

(ii) Laboratory studies. Serum liver enzyme activities are increased. Urine, milk, and blood may contain detectable levels of aflatoxin during acute exposure, and the toxin is readily detected in feed.

(b) Chronic aflatoxicosis. It may be difficult to link subtle effects of growth suppression, poor feed efficiency, and impaired immune function to previous aflatoxin exposure, because contaminated feed that initiated chronic events may no longer be present and tissue residues may be too low to be detected by routine methods. Therefore, chronic aflatoxicosis often goes undiagnosed.

(5) Therapeutic plan. Aflatoxicosis presents as a herd problem and intensive individual animal therapy is not practical.

(a) Suspect feed should be removed and a high-quality protein diet supplemented with vitamins A, D, E, K, and B complex should be provided to counteract the effect of aflatoxin on protein and vitamin utilization.

(b) There are no specific antidotes, but in acute cases of experimentally induced aflatoxicosis, goats treated with L-methionine (200 mg/kg orally every *8* hours) and sodium thiosulfate (50 mg/kg orally every *8* hours), had improved survival.

(c) Because animals exposed to aflatoxin may have compromised immune systems, clinical signs of infectious disease should be aggressively treated with antimicrobial therapy.

(6) Prevention

(a) Proper feed storage is indicated to prevent mycotoxicosis; the maximum safe moisture content of cereal grains is 14%. High-moisture grains can be stored by excluding air or adding preservatives (e.g., propionic acid).

(b) Aflatoxin-contaminated corn can be detoxified by treatment with ammonia, but this is a costly and impractical procedure.

(c) Aflatoxin-contaminated feed can be diluted with normal feed, but this practice is risky because when low levels of aflatoxin are potentially harmful.

b. PA toxicosis (see also II A 2). Signs of PA toxicosis in cattle include diarrhea, weight loss, a prolapsed rectum, ascites, and subtle neurologic signs. Icterus is uncommon. Calves are more susceptible to PA toxicosis than mature cattle.

c. Copper toxicosis is an acute, highly fatal hemolytic crisis affecting primarily sheep. It is associated with the sudden massive release of hepatic copper stores that have accumulated over a prolonged period as the result of excessive copper intake. Liver necrosis, which occurs secondary to copper accumulation, precedes the onset of hemolysis.

d. Halothane toxicosis. Halothane gas anesthesia is commonly used without complications in goats, but there have been two reports of presumed halothane toxicity causing massive hepatocellular necrosis and signs of hepatoencephalopathy a few days after administration of anesthesia.

B. Hepatobiliary diseases of calves, lambs, and kids

1. **Portosystemic** anomalies are rarely diagnosed in calves.

a. Clinical findings. Clinical signs include stunted growth and various episodic manifestations of hepatoencephalopathy.

b. Diagnostic plan

(1) Laboratory studies. Hyperammonemia, delayed sulfobromopthalein clearance, and increased bile acid concentrations, without alterations in serum liver enzyme activity, suggest a diagnosis of portosystemic shunt.

(2) Liver biopsy. The only abnormality on liver biopsy is mild periportal fibrosis.

(3) Imaging studies. Diagnosis is confirmed using ultrasound or intraoperative mesenteric **portography.**

c. Therapeutic plan. Successful surgical correction has been reported.

2. Hepatic abscesses in neonatal ruminants can be a complication of an umbilical vein abscess.

3. Congenital diseases

a. Dubin-Johnson syndrome is an autosomal recessive condition of Corriedale sheep characterized by a defect in biliary excretion of conjugated bilirubin and phylloerythrin.

(1) Patient profile and history. This syndrome affects 6-month-old Corriedale lambs on green feed.

(2) Clinical findings include anorexia, icterus, and severe photodermatitis.

(3) Diagnostic plan

(a) Laboratory studies. Biochemical abnormalities include conjugated hyperbilirubinemia and delayed sulfobromopthalein clearance.
(b) Liver biopsy reveals brown to black granules in hepatocytes with normal hepatic archite'cture.
(4) Therapeutic plan. Affected animals may survive if exposure to sunlight is avoided, but this approach may be impractical and affected lambs are usually culled.
(5) Prevention. Selective breeding reduces the incidence of disease.

b. Gilbert's syndrome is inherited as an autosomal recessive trait and is characterized by a failure of hepatic uptake of bilirubin and phylloerythrin. Renal failure accompanies this condition.
(1) Patient profile and history. This syndrome affects 6-month-old Southdown sheep on pasture.
(2) Clinical findings. Photodermatitis, without icterus, resulting in ulcerative lesions around the mouth and ears is the usual clinical presentation.
(3) Diagnostic plan
(a) Laboratory studies. Findings include unconjugated hyperbilirubinemia (exacerbatedby fasting), delayed sulfobromopthaleinclearance, and azotemia.
(b) Liver biopsy. Histologic evaluation of liver biopsy specimens usually reveals no abnormalities.
(4) Therapeutic plan. Affected sheep should be kept out of sunlight to prevent photodermatitis.
(5) Prevention. Affected sheep and their dams and sires should not be retained for breeding purposes.

IV. HEPATOBILIARY DISEASES OF SWINE

A. Ascariasis

1. Patient profile and history
   a. Patient profile. Ascariasis affects young growing pigs up to 5 months of age.
   b. History. There is usually a complaint of poor growth.

2. Clinical findings. An occasional cough may be noted in pigs infected with ascarids. In rare cases of massive infestation, pigs exhibit severe dyspnea or die of acute hepatic insufficiency. Adult worms may be vomited; occasionally, intestinal obstruction and rupture or obstructive jaundice are seen.

3. Etiology and pathogenesis
   a. Etiology. Roundworms (*Ascaris suum*), the cause of ascariasis, are found in most swine-producing regions.
   b. Pathogenesis
   (1) A. *suum* begins its life cycle with eggs shed by adult worms. In warm conditions, infective second-stage larvae hatch from the eggs in 10–14 days. Ingested larvae penetrate the intestine and are carried via the portal circulation to the liver. Migration through the liver to the lungs is completewithin 1 week. Within 2 weeks of ingestion, migration to the trachea is complete. Larvae are swallowed and develop to adults in the intestine. Egg production by adults commences 6–9 weeks post infection.
   (2) Larval migration through the liver leaves characteristic white foci of fibrosis. Initially, the liver lesions are caused by the migration of the larvae; subsequent exposure causes damage following an antigen–antibody reaction. Lesions generally heal 35 days after migration.
   (3) Immunity to roundworm infection develops first in the lungs, resulting in decreased lung larval counts. Liver and gut immunity take longer to develop. Under natural conditions, liver lesions occur until the pig weighs approximately 90 kg. In pigs older than 2 years, full gut immunity prevents larvae from reaching the liver.

4. Diagnostic plan. Fecal flotation can detect the presence of ascarid eggs in feces.

5. Therapeutic plan. **Ivermectin,** levamisole, and pyrantel tartrate are effective anthelmintics.

6. Prevention. Because exposure to ascarids during the growing phase may permanently affect growth rate and feed conversion and add 5%–13% to the cost of production to market, and liver lesions caused by ascarid migration create losses in the meat packing industry, prevention of disease is important.
   a. Monitoring of **ascarid** burdens. Annual examination of five to ten fecal samples from all categories of pigs is recommended. Liver inspection at slaughter can be used to monitor ascarid burdens on farms.
   b. Disinfection of living spaces. If pigs are confined to concrete pens, normal hygienic precautions will decrease the risk of ascariasis. Farrowing pens should be cleaned with a pressure sprayer.
   c. Prophylactic anthelmintic therapy may be indicated for piglets until they are weaned.
   (1) If sows are dewormed prior to being placed in a farrowing pen cleaned with a pressure sprayer, prophylactic anthelmintic treatment for piglets may not be required.
   (2) Periodic or continuous low level treatments with anthelmintics may be required if hygiene is poor.
   d. Prevention of exposure. Early weaning of piglets (at 3–4 weeks of age) will remove them from a potentially infective environment (*Ascaris* ova require 30–35 days to reach infectivity in a farrowing house environment).

B. Hepatosis dietetica

occurs in rapidly growing pigs 2–16 weeks of age. It is caused by vitamin E and selenium deficiency. Lesions include subcutaneous edema, transudate in serous cavities, and hepatocellular necrosis with hemorrhage.

C. Aflatoxicosis

(see also III A 6 a) Swine are more susceptible than cattle to the effects of aflatoxins. As with cattle, young swine are more susceptible than adults. The main target organ is the liver; affected pigs may die of acute liver failure or exhibit signs of ill thrift.

STUDY QUESTIONS

DIRECTIONS: Each of the numbered items or incomplete statements in this section is followed by answers or by completions of the statement. Select the ONE numbered answer or completion that is BEST in each case.

1. Which one of the following statements concerning liver failure in large animals is true?

(1) Pale feces suggest significant bile duct obstruction in suckling herbivores.
(2) Ascites is a common finding in horses with acute liver failure.
(3) A hemolytic crisis is a frequent complication of liver failure in ruminants.
(4) Hyperammonemia is the only metabolic alteration responsible for hepatic encephalopathy.
(5) Hypoalbuminemia is a consistent finding in horses and ruminants with liver failure.

2. Which one of the following is appropriate dietary management for an equine patient exhibiting signs of hepatic encephalopathy?

(1) Feeding high-quality alfalfa or legume hay
(2) Force feeding an alfalfa meal and cottage cheese slurry
(3) Withholding feed and administering 50% dextrose intravenously
(4) Feeding a mixture of beet pulp and cracked corn
(5) Feeding a bran mash with added mineral oil

3. Which one of the following statements pertaining to serum hepatitis (Theiler's disease) of horses is true?

(1) Serum hepatitis is caused by the hepatitis B virus.
(2) Serum hepatitis is most commonly diagnosed in lactating mares.
(3) Serum hepatitis is attributed to tetanus toxoid administration.
(4) Serum hepatitis is usually diagnosed in the winter months.
(5) Serum hepatitis is a disease with high morbidity and low mortality rates.

4. A veterinarian is called to a farm to examine a 5-year-old pony mare. The mare was bred 310 days ago and has been anorexic and depressed for 2 days. Recently, the owner restricted her feed intake because she was diagnosed as having laminitis. A jugular venous sample is obtained; the plasma has a milky appearance. What is the most likely diagnosis?

(1) Hyperlipidemia
(2) Pregnancy hypercalcemia
(3) Abdominal fat necrosis
(4) Pregnancy toxemia
(5) Tyzzer's disease

5. Which one of the following statements regarding pyrrolizidine alkaloid (PA) toxicosis in large domestic animals is true?

(1) Cattle are more resistant to PA toxicosis than are sheep and horses.
(2) Cattle, sheep, and horses are equally susceptible to PA toxicosis.
(3) Sheep are more resistant to PA toxicosis than are cattle and horses.
(4) Horses are more resistant to PA toxicosis than are sheep and cattle.
(5) Cattle, sheep, and horses are equally resistant to PA toxicosis.

6. Which one of the following statements regarding hepatic abscesses in feedlot cattle is true?

(1) They are a common cause of diffuse peritonitis.
(2) Common clinical manifestations include epistaxis and hemoptysis.
(3) The presentation is subclinical in most cases.
(4) They are a common cause of septic shock.
(5) They usually cause obstructive icterus (as a result of bile duct occlusion).

7. Inherited icterus and photosensitization have been reported in 6-month-old:

(1) Corriedale and Southdown lambs.
(2) Dorset and Corriedale lambs.
(3) Finn and Dorset lambs.
(4) Hampshire and Southdown lambs.
(5) Merino and Suffolk lambs.

8. Which one of the following treatments is contraindicated in a donkey suffering from hyperlipidemia?

(1) 5% Dextrose intravenously
(2) Anabolic steroids
(3) Insulin
(4) Glucocorticoids
(5) Heparin

9. Which one of the following anthelmintics will treat both *Ostertagia circumcincta* and *Fasciola* hepatica infestation in beef cattle?

(1) Albendazole
(2) Fenbendazole
(3) Clorsulon
(4) Ivermectin
(5) Morantel

DIRECTIONS: The numbered item in this section is negatively phrased, as indicated by a capitalized word such as NOT, LEAST, or EXCEPT. Select the ONE numbered answer or completion that is BEST.

10. Which one of the following is NOT hepatotoxic to large domestic animals?

(1) *Quercus*
(2) *Senecio*
(3) *Amsinckia*
(4) *Crotolaria*
(5) *Aspergillus* flaws

ANSWERS AND EXPLANATIONS

1. The answer is 1 [I B 1 c (5)]. Pale feces are a likely finding in suckling ruminants with biliary obstruction because stercobilin, a bilirubin metabolite excreted in the bile, is responsible for fecal color and would not be present in the feces of animals with significant biliary obstruction. Ascites is a common finding in cattle with hepatic cirrhosis, but is rarely reported in horses. A terminal hemolytic crisis, associated with increased red blood cell (RBC) fragility, has been reported in horses, but not in cattle, with terminal liver failure. A multitude of metabolic derangements contribute to the development of hepatic encephalopathy, not just hyperammonemia. Hypoalbuminemia is an uncommon finding in large animal patients with hepatic encephalopathy.

2. The answer is 4 [I C 1 b (3) (a)]. A high-energy, low-protein diet rich in branched-chain amino acids is recommended for horses with liver failure and signs of hepatic encephalopathy. A mixture of two parts beet pulp and one part cracked corn in molasses is often used. Feeding of a high-quality alfalfa or legume hay or force feeding an alfalfa meal and cottage cheese slurry would be inappropriate because both of these diets are high in protein. The goal is to limit protein consumption, because protein serves as a substrate for ammonia production by intestinal bacteria. Feed should not be withheld, and 5% (not 50%) dextrose should be administered. Higher concentrations of dextrose will cause glucosuria and dehydration. A bran mash diet is too low in energy to be offered as the primary feed source.

3. The answer is 2 [I I A 1]. Lactating mares appear to be at higher risk for serum hepatitis (Theiler's disease) due to the common practice of administering tetanus antitoxin (TAT) postpartum. There is speculation that a virus, similar to the hepatitis B virus that affects humans, causes serum hepatitis in horses, but this theory remains to be proven. Serum hepatitis usually occurs 4–10 weeks after the administration of TAT, not tetanus toxoid. Serum hepatitis occurs most often in the summer and fall, and is characterized by low morbidity rater (2%–18%), but high mortality rates (greater than 60%).

4. The answer is 1 [II A 4]. Ponies in advanced gestation are prone to developing hyperlipidemia when fasted. The milky (lipemic) plasma supports this diagnosis. Pregnancy hypercalcemia, abdominal fat necrosis, and pregnancy toxemia do not occur in horses. Tyzzefs disease occurs only in foals.

5. The answer is 3 [II A 2 a]. Sheep are more resistant than cattle and horses to pyrrolizidine alkaloid (PA) toxicosis. For this reason, sheep are often used to graze pastures with PA-containing plants, which would be unsafe for cattle and horses.

6. The answer is 3 [III A 1]. Hepatic abscesses may occur in up to 40% of feedlot cattle and are usually an incidental finding at slaughter. Diffuse peritonitis, epistaxis and hemoptysis, septic shock, and bile duct occlusion leading to obstructive icterus are uncommon sequelae of hepatic abcessation in feedlot cattle.

7. The answer is 1 [III B 3]. Dubin-Johnson syndrome of Corriedale sheep and Gilbert's syndrome of Southdown sheep are hereditary diseases characterized by icterus and photodermatitis. Six-month-old lambs on pasture are affected.

8. The answer is 4 [II A 4 e]. Glucocorticoids are contraindicated in the treatment of a donkey with hyperlipidernia because they induce activity of hormone-sensitive lipase, which will further stimulate lipolysis. The administration of 5% dextrose, anabolic steroids, insulin, and heparin is appropriate, although the efficacy of insulin and heparin have been questioned.

9. The answer is 3 [III A 2 e (2)]. Albendazole is a broad-spectrum flukicide that is effective against liver flukes, such as *Fasciola* hepatica and nematodes, such as *Ostertagia circumcincta*. Fenbendazole, ivermectin, and morantel are not efficacious against liver flukes. Clorsulon is a narrow-spectrum flukicide that will eliminate liver flukes, but not gastrointestinal nematodes.

10. The answer is 1 [III A 6]. *Quercus* (oak) is nephrotoxic, not hepatotoxic. Senecio, Amsinckia, and *Crotolaria* contain pyrrolizidine alkaloids (PAs), which are hepatotoxic. *Aspergillus flavus* produces aflatoxin, which is also hepatotoxic.